Gout

Disclaimer

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**Red Flags**

- Septic arthritis

**Background – About Gout**

Gout is due to the deposition of monosodium urate crystals within and around joints, causing acute inflammation and eventual tissue damage.

- Diagnosis is made by demonstration of urate crystals in synovial fluid or tophi.
- In patients with gout, the most common cause of hyperuricaemia is under-excretion of uric acid. A minority of patients are over-producers of urate.
- The duration and magnitude of hyperuricaemia is directly correlated with the likelihood of developing gouty arthritis and uric acid kidney stones. Gout can occur in people with normal plasma urate.
- The prevalence of gout is higher in the Aboriginal population.
- Prevalence is 1.74% of all adults in Australia. This increases with age to 4 to 6% of people aged > 50 years.
- Gout is an independent risk factor for cardiovascular disease.
- Many people with hyperuricaemia never develop gout. There is currently no evidence to support urate-lowering therapy in patients with asymptomatic hyperuricaemia.
- The mainstay of gout treatment is prevention through lifestyle modifications and urate lowering therapy.
- The aim of urate-lowering therapy is to lower serum uric acid to a concentration that:
  - dissolves existing monosodium urate crystals in the joints, soft tissues and kidneys and prevents the formation of new crystals.
  - reduces the frequency and severity of acute attacks, eventually leading to the absence of acute attacks.
  - resolves tophi.

**Assessment**

1. History – ask about:
   - distribution of **joint involvement**.

   **Distribution of joint involvement**
   - First metatarsophalangeal (MTP) joint is involved in 50% of all attacks, and 70% of first attacks.
   - Other common joints are knee, midfoot, wrist, ankle, finger, and elbow.
   - Usually monoarticular or oligoarticular (< 4 joints). Can be polyarticular, affecting multiple joints in the hands and feet, especially in older people.

   - systemic symptoms, fever, and malaise (common).
➢ **history of attacks** including severity, frequency and duration of symptoms. Gout usually presents as episodes of exquisitely painful joint(s) with swelling, erythema and heat that lasts 1 to 3 weeks but is normal in between episodes.

**History of attacks**
- A typical history is rapid onset of usually severe pain (usually occurring overnight when the temperature is lower) in the distal extremities with exquisite tenderness to light touch or pressure, and difficulty moving the joint.
- There is limitation of function due to pain and stiffness, including morning stiffness and there may be erythema of the overlying skin.

➢ **precipitating factors.**

**Precipitating factors**
- High protein foods, especially shellfish, offal, and yeast extracts
- Alcohol, especially in excess
- Soft drinks flavoured with fructose
- Dehydration
- Trauma
- New medications e.g., diuretics
- Recent surgery, physical stress, or infection

➢ **risk factors**

**Risk factors**
- Male gender
- Older age – peaks in men between ages 40 to 60 years, and women between ages 50 to 70 years
- Menopausal status – gout especially rare in premenopausal women
- Elderly women on diuretics – can present with a rapidly progressive form of gout, that can result in rapidly growing tophi and destructive arthropathy particularly of the fingers
- Family history
- Māori or Pacific Islander heritage
- Aboriginal and Torres Strait Islanders heritage
- Consumption of meat, seafood, alcohol
- Medications including diuretics, aspirin, tacrolimus, cyclosporin
- Conditions with a high cell turnover rate, e.g., psoriasis, myeloproliferative disorders, chemotherapy-induced cell death

➢ previous and current treatment.
➢ compliance with both medical and lifestyle management.
➢ effect of symptoms on activities of daily living e.g., work, study, or carer role.

1. **Examination:**
   ➢ Check for fever
   ➢ Examine **involved joints:**
     - Swelling and joint effusion
     - Erythema and warmth (may be subtle at times)
     - Prominent diffuse joint tenderness
Between episodes there is no residual swelling, effusion, erythema, tenderness or warmth.

➢ Check for signs of **chronic tophaceous gout**.

**Chronic tophaceous gout**

Chronic tophaceous gout is an end-stage form of gout, which occurs if recurrent gout remains untreated or incompletely managed over an extended period of time (5 to 10 years) with urate-lowering medication. Features include:

- development of **tophi**

  **Tophi**
  - Tophi are yellow-white subcutaneous nodules, which are often soft and non-tender.
  - Commonly over the extensor surface of joints, especially elbows, knees and Achilles tendon. May also be evident over dorsal aspects of hands and feet and in helix of the ears.
  - more frequent attacks
  - increase in the number of joints affected
  - gradual worsening of inflammatory arthritis and erosive joint damage
  - urate nephropathy
  - renal calculi.

2. Consider differential diagnoses:

➢ **Septic arthritis** – both gout and septic arthritis can present as a single swollen painful joint over a 6 to 12 hour period.
  - Although a low-grade fever can occur with gout, fever with monoarticular arthritis should be treated as septic arthritis until proven otherwise.
  - Joint aspiration is needed to definitively exclude septic arthritis (see below).

➢ **Chondrocalcinosis** (pseudogout)
  - Occurs in up to 20 to 30% of elderly with generalised osteoarthritis and patients may have low level inflammatory signs.
  - Management is similar to acute gout although NSAIDs are often contra-indicated due to co-morbidities.
  - Alternative treatments are prednisone 20 to 40 mg daily, tapering over two weeks, or colchicine 0.5 mg twice daily.

➢ **Inflammatory arthritis**

3. Investigations:

➢ Arrange **joint aspiration**. Always perform unless good reason not to.

**Joint aspiration**

- Joint aspiration can be performed on most joints, but is more difficult for smaller joints.
- Contraindications:
  - Overlying cellulitis
  - Joint prosthesis
• Can be done in general practice, under radiological guidance, or referred to the emergency department.
• If done in general practice, send fluid for:
  o cell count (EDTA tube. Use a paediatric tube if only small volume of aspirate)
  o culture (blood culture bottle).
• The presence of monosodium urate crystals confirms the diagnosis. The white cell count usually exceeds 2.0 x 10^9/L and are mostly polymorphonuclear cells (PMN)

➢ Arrange renal function testing, if not performed within 3 months.
➢ Measure uric acid during the attack as well as a baseline, inter-episode serum uric acid. During an acute attack, levels are normal in up to 50% of patients. It becomes more reliable 2 weeks after an acute attack.
➢ Consider arranging X-ray and ultrasound scans for differential diagnosis.

4. Screen for any other conditions associated with gout.

Conditions associated with gout
• Hypertension
• Cardiovascular disease
• Renal impairment
• Diabetes
• Obesity
• Hyperlipidaemia

Management

Acute management

1. If acute gout:
   ➢ and there is fever and acute monoarthritis, or signs of sepsis, refer for immediate rheumatology assessment for exclusion of septic arthritis.
   ➢ provide symptom relief with anti-inflammatory medications depending on age, renal function, and co-morbidities. Avoid using narcotics, as they are not effective for gout.

   Symptom relief for acute gout
   • Consider first-line treatment with:
     o non-steroidal anti-inflammatory drugs (NSAIDs), and consider adding a proton-pump inhibitor.

   Non-steroidal anti-inflammatory drugs (NSAIDs)
   Prescribe appropriate NSAIDS, e.g., naproxen 500 mg twice daily.
   ▪ Use NSAIDs in the lowest effective dose for the shortest period of time.
   ▪ Avoid NSAIDs in older adults or if cardiac or renal disease.
Consider the "triple whammy" combination of an ACE, diuretic, and NSAID, which may cause increased blood pressure and renal impairment.

- **low-dose colchicine.**
  - Use low-dose regimens as high doses can be fatal. Colchicine has a narrow therapeutic margin and considerable variation in absorption between individuals.
  - Start within 24 hours of attack.
  - Give 0.5 mg twice daily. Reduce to 0.5 mg if not tolerated, due to gastrointestinal adverse effects (usually diarrhoea).
  - For interactions and contraindications, see NPS MedicineWise – [Colchicine for Acute Gout](#).

- If NSAIDs and colchicine are contraindicated or the patient is elderly, use corticosteroids, e.g. prednisolone:
  - Usually, give prednisolone 20 to 40 mg daily until the episode resolves.
  - Once resolved, reduce the dose over one to two weeks.

- If 1 or 2 joints are affected, consider intra-articular corticosteroids, e.g. triamcinolone acetonide (Kenacort-A). The dose depends on the joint size.

3. If the response to treatment is poor, check compliance and reconsider diagnosis.
   - Consider **joint aspiration** to confirm diagnosis and exclude co-existing infection.
   - Consider [rheumatology advice](#).

4. Consider starting allopurinol at any time so long as commenced on a low dose (50 mg daily), and **flare prophylaxis** is given concomitantly. See ongoing management. If the patient is already taking allopurinol or other urate-lowering therapy, advise them to continue.

**Flare prophylaxis**

- Use:
  - non-steroidal anti-inflammatory drugs (NSAIDs) at the lower end of the dosing schedule, or
  - colchicine 500 micrograms orally, once or twice daily. Reduce the dose in renal impairment and reduce dose or stop if develop diarrhoea.

- Continue flare prophylaxis for 3 to 6 months after the target serum urate is achieved. If patient is having frequent attacks, use oral steroid (5 to 10 mg per day of prednisolone).

5. Arrange follow-up for preventative treatment (as below).

6. Arrange an [urgent or routine rheumatology referral](#) if:
   - diagnosis is uncertain or presentation atypical, including:
     - suspected gout in premenopausal women.
     - men aged < 40 years.
   - complex co-morbidities.
   - eGFR < 30 ml/L.
   - solid organ transplant.
Ongoing management

Long-term management of gout focuses on controlling the underlying hyperuricaemia, aiming for a target serum urate level of < 0.3 mmol/L in order to prevent flares and achieve regression of tophi.

1. Provide education and advice on *lifestyle interventions.*

2. Arrange **urgent or routine rheumatology referral** if:
   - complex co-morbidities.
   - solid organ transplant.
   - renal impairment with eGFR < 30mL/min.

3. For all patients, consider **indications for urate-lowering therapy.**

   **Indications for urate-lowering therapy**
   - Recurrent gout (2 or more attacks per year)
   - Gouty tophi
   - Chronic gouty arthritis
   - Evidence of damage on X-ray
   - Early-onset gout, strong family history, and serum urate greater than 0.6 mmol/L

   *In patients with asymptomatic hyperuricaemia, there is no evidence to support urate-lowering therapy.*

4. Determine target serum urate level i.e., below 0.36 mmol/L, or if tophi present, below 0.30 mmol/L.

5. Start urate-lowering therapy with allopurinol, using a **treat-to-target approach.** Always prescribe **flare prophylaxis** when starting allopurinol or other urate lowering medications:

   **Treat-to-target approach**
   - Aim for a serum urate target of < 0.3 mmol/L.
   - Start dose at 50 mg orally once a day.
   - Measure serum urate after 2 weeks and increase dose by 50 to 100 mg if above target.
   - Continue to monitor serum urate and titrate dose every 2 weeks until target is reached.
   - The patient may need up to 900 mg allopurinol to achieve target.
   - Monitor UEC monthly during titration process, or for patients with renal impairment, with every dose increase.
   - Monitor FBE and LFTs every 3 months during the titration process.
   - Once at target, measure serum urate, LFTs, and renal function every 6 to 12 months.
   - Maintain flare prophylaxis for 3 to 6 months after target serum urate is achieved.
   - Manage ongoing attacks during the titration period with low dose NSAIDs or prednisolone.
   - Educate patients about the aim of urate lowering therapy and what to expect. This will increase the chances of compliance.
   - Warn patients it can take more than 12 months after reaching their target for gout attacks to stop, and years for tophi to dissolve.

   ➢ If eGFR below 30, arrange for **urgent or routine rheumatology referral.**
   ➢ Warn patients to cease allopurinol if they develop a rash. Severe hypersensitivity usually occurs in the first 6 weeks and is associated with rash.
➢ Consider **HLA–B*5801 screening** before starting allopurinol in **Asian subpopulations**.

**Asian subpopulations**
- Consider HLA–B*5801 screening as part of risk management in Asian subpopulations where there is increased frequency of the HLA–B*5801 allele.
- The HLA–B*5801-positive subpopulations have a very high risk for severe allopurinol hypersensitivity reaction, e.g. Koreans with chronic kidney disease stage 3 or worse, and all those of Han Chinese and Thai descent.

**HLA-B*5801 screening**
Cost is approximately $75 with no Medicare rebate

➢ If serum urate fails to reduce, always check compliance.
➢ If any concerns, seek [rheumatology advice](#).
➢ If allopurinol is contraindicated, not tolerated, or ineffective, consider [urgent or routine rheumatology referral](#) or alternative urate-lowering medications e.g., **Febuxostat**.

**Febuxostat**
- Consider febuxostat if allopurinol failure, intolerance, or contraindication.
  - Failure means failure to reach target serum urate. Flare of gout when starting allopurinol does not constitute intolerance or failure of allopurinol.
  - Febuxostat is available – PBS authority required
- Patients who get a rash or hypersensitivity on allopurinol or have renal disease may have hypersensitivity reactions with febuxostat. These can be serious. Most cases occur during the first month of treatment.
- Avoid combination with azathioprine, as they may interact.
- Provide appropriate prophylaxis against gout flare with non-steroidal anti-inflammatory drugs (NSAIDs), colchicine, or prednisolone. Patients starting febuxostat tend to have frequent gout flares.
- Check liver function before starting, after 2 weeks, then monthly. There is a risk of hepatotoxicity (including fatal events) with febuxostat.
- Many of the patients who can tolerate febuxostat have co-morbidities and medications which make prescribing difficult. Consider [urgent or routine rheumatology referral](#).

6. Seek [rheumatology advice](#) or refer for [urgent or routine rheumatology referral](#) if:
- intolerance to urate-lowering medications.
- renal impairment, co-morbidities, and medications which affect the choice of urate-lowering therapies.

7. If **failure to respond** to urate-lowering medications, check compliance. If good compliance, at maximally tolerated dose of urate lowering medications, and ongoing symptoms, seek [rheumatology advice](#) or arrange [urgent or routine rheumatology referral](#). Referral is not necessary for asymptomatic hyperuricaemia.
**Failure to respond**
- Serum urate remains above target and ongoing symptoms
- Recurrent attacks
- Progressive joint damage
- Tophaceous gout with active symptoms or growing tophi despite medical management

Manage any other *Conditions associated with gout*


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### Referral

- If acute gout and there is fever and acute monoarthritis, or signs of sepsis, refer for [immediate rheumatology assessment](#) for exclusion of septic arthritis.
- If poor response to treatment for acute gout, seek [rheumatology advice](#).
- Arrange [urgent or routine rheumatology referral](#) if:
  - diagnosis is uncertain or presentation atypical, including:
    - suspected gout in premenopausal women.
    - men aged < 40 years.
  - complex co-morbidities.
  - eGFR < 30 ml/L.
  - solid organ transplant.
  - *failure to respond* to urate-lowering medications despite good compliance.
  - intolerance to urate-lowering therapies (e.g., rash, hepatitis).
  - ongoing symptoms despite maximum tolerated allopurinol dosage.
  - progressive joint damage despite medical management.
  - tophaceous gout with active symptoms, or growing tophi, despite medical management.

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### Information

#### For health professionals

Further information
- Australian Family Physician – [The Management of Gout: Much Has Changed](#).
- Australian Prescriber – [The Management of Gout: Urate-Lowering Therapy](#).

#### For patients

- Arthritis Australia – Gout:
  - [Gout](#)
  - [Gout and Diet](#)
- Australian Rheumatology Association:
  - [NSAIDs](#)
  - [Prednisolone & Prednisone](#)


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